ORIGINAL ARTICLE

Body Mass Index, Waist Circumference, and the Risk of Type 2 Diabetes Mellitus

Implications for Routine Clinical Practice

Silke Feller, Heiner Boeing, Tobias Pischon

SUMMARY

Background: Current guidelines for assessing the risk of developing type 2 diabetes mellitus (DM) recommend using the patient's body-mass index (BMI) as a primary measure. Waist circumference measurement is recommended for overweight or obese patients only (BMI ≥ 25).

Methods: We studied the interaction between BMI and waist circumference with respect to the risk of developing type 2 DM in a cohort of 9753 men and 15491 women, aged 35 to 65, who participated in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam. The statistical analysis was performed with multivariable-adjusted Cox proportional hazard regression.

Results: During a mean follow-up interval of 8 years, type 2 DM was newly diagnosed in 583 men and 425 women. A statistically significant interaction was found between BMI and waist circumference with respect to the risk of type 2 DM ($p<0.0001$). The positive association between waist circumference and diabetes risk was stronger in persons with lower BMI. The relative risk (RR) of developing type 2 DM among persons of low or normal weight (BMI < 25) who had a large waist circumference was at least as high as that among overweight persons (BMI 25–29.9) with a small waist circumference: for the first case, the RR was 3.62 [1.67–7.83] in men and 2.74 [1.52–4.94] in women; for the second case, the RR was 2.26 [1.51–3.37] in men and 1.40 [0.61–3.19] in women (The figures in square brackets are 95% confidence intervals). These relative risks were calculated in comparison to the risk among persons of low or normal weight (BMI < 25) with a small waist circumference.

Conclusion: These findings imply that the waist circumference is an important additional piece of information for assessing the risk of type 2 DM, particularly among persons of low or normal weight.

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It is generally accepted that overweight and obesity are important in the development of type 2 diabetes mellitus. Obesity is understood as an abnormal increase in body fat. This is measured in practice using the body mass index (BMI), i.e., the weight in kilograms divided by the square of the height in metres. The guidelines of the German Obesity Society (1) and the World Health Organization (2) define overweight as a BMI of at least 25 kg/m^2. BMI between 25 and 29.9 25 kg/m^2 is defined as pre-obesity; BMI of at least 30 kg/m^2 is defined as obesity. The classifications in the USA guidelines (3) are slightly different *(Table 1)*.

Although the BMI captures the degree of overweight and obesity, it ignores body fat distribution. For example, visceral fat tissue is metabolically more active than non-visceral fat and secretes more hormones and cytokines, which may be important for the development of diabetes (4, 5). Measuring waist circumference is a simple means of assessing the levels of visceral fat. Increased waist circumference is also closely associated with an increased risk of diabetes (6). However, current obesity and diabetes guidelines only recommend that waist circumference should be measured from a BMI of 25 kg/m^2 (1–3), as this is the level at which the increased risk is thought to start *(Table 1)*.

However, assessing risk on the basis of anthropometric parameters is not easy, as there is a strong correlation among these markers. As overweight and obesity are among the strongest known risk factors for type 2 diabetes, risk statements based on anthropometric measurements should be as precise as possible and allow for the complex interactions between these parameters. The objective of the present study was therefore to examine how the risk for type 2 diabetes can best be described by measuring BMI and waist circumference. This investigation was part of the EPIC Potsdam study, one of the largest prospective population-based cohort studies in Germany.

Methods

Study population

The European Prospective Investigation into Cancer and Nutrition (EPIC) Potsdam study is a part of a prospective Europe-wide study investigating the links

TABLE 1

Current classifications of overweight and obesity according to DAG, DDG, DGEM, WHO, or ADA

Classifications of obesity				Diabetes risk*[1]*[2]	
DAG, DDG, DGEM, WHO*[1]	American Diabetes Association*[2]	BMI (kg/m^2)	Obesity class	Waist: men ≤102 cm women ≤88 cm	Waist: men >102 cm women >88 cm
Underweight	Underweight	< 18.5			
Normal weight	Normal weight	18.5–24.9			
Overweight		≥ 25			
Pre-obesity	Overweight	25.0–29.9		increased	high
Obesity	Obesity	30.0–34.9	I	high	very high
		35.0–39.9	II	very high	very high
Extreme obesity		≥ 40	III	extremely high	extremely high

*[1] DAG, German Obesity Society; DDG, German Diabetes Society; DGEM, German Society for Nutritional Medicine (1); WHO, World Health Organization (2);
*[2] ADA, American Diabetes Association (3)

between nutrition, lifestyle and the incidence of chronic diseases. Between 1994 and 1998, 27 548 persons (including 16 644 women), from Potsdam and surroundings, aged from 35 to 65 years, were included in the study. The basic investigations included anthropometric measurements, personal interviews, and completion of questionnaires on lifestyle, nutrition and sociodemographic characteristics (7). 22.3% of the invited persons were recruited into the study. All participants were informed of the nature of the study and signed an informed consent form. The Ethics Committee of the Brandenburg State Medical Association approved the project.

Persons were excluded from our analysis who self-reported a diabetes diagnosis at baseline, as well as those with incomplete follow-up, or missing anthropometric or covariable data or without medical confirmation of diabetes during the follow-up period. Data from 9753 men and 15 491 women were available.

Recording of new cases of type 2 diabetes

New (incident) cases of type 2 diabetes mellitus were identified on the basis of the information provided by the study participant on the forms about diagnosis, medication, or treatment of type 2 diabetes mellitus. These cases were identified by contact with the responsible physicians. The presence of type 2 diabetes was confirmed by classification E11 in accordance with ICD-10 and the date of the first diagnosis was recorded.

Anthropometrics and other variables

The anthropometric measurements were performed by trained personnel under standardized conditions, following the recommendations of the World Health Organization. The participants wore only light underclothes for these measurements (8). Body weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm. Waist circumference was measured at the midpoint between the lower rib and iliac crest (8, 9). Level of education, highest school qualification, physical stress at the workplace, and alcohol consumption were recorded with a questionnaire. Medical history, general physical activity, and smoking habits were recorded in personal interviews. Physical activity was expressed as PAL (physical activity level), calculated as a person's total energy expenditure (i.e. the sum of the products of duration and intensity of individual activities such as sport, housework, gardening, manual work, climbing stairs, walking, running or cycling) over 24 hours. The intensity was calculated in the form of metabolic equivalents (METs). Television and sleeping habits of the participants and seasonal differences in activity were also considered (10). One MET is equivalent to energy consumption when sitting still.

Statistical analysis

Relative risks and 95% confidence intervals were calculated separately for each sex by Cox proportional hazard regression (11). The age of the participant was taken as the time at risk. The time of entry was the age at recruitment. The time of exit was defined as the age at diagnosis of type 2 diabetes or the last follow-up (censoring) (12, 13). The analysis was stratified by age (STRATA statement in PROC PHREG in SAS) and adjusted for height (continuous), smoking habits (never smoked, ex-smoker, smoker), alcohol consumption (0.0–5, 5–10, 10–20, 20–40 or >40g/day), physical activity (continuous), level of education (in education, no school qualification or semiskilled worker, skilled worker, technical college leaving exam, technical university or university qualification), highest school qualification (no school qualification, completion of the 8th class, completion of the 10th class, qualification to enter a technical university, qualification to enter a university) and physical stress at the workplace (light, moderate, intense). Waist circumference and BMI were

TABLE 2

Characteristics of the 25 244 participants in the EPIC Potsdam Study at screening

	Men (n = 9753)	Women (n = 15 491)
Age (years)*1	52 (8)*1	49 (9)
BMI (kg/m^2)*1	26.9 (3.5)	25.6 (4.6)
Waist (cm)*1	94.4 (9.9)	80.2 (11.2)
Height (cm)*1	175.0 (6.7)	163.0 (6.2)
Physical activity level (PAL)*1	1.6 (0.3)	1.6 (0.2)
Smoking habits (%)		
– never smoked	31	58
– ex-smoker	44	24
– smoker	25	18
Highest school qualification (%):		
– completion of the 8th class	24	27
– completion of the 10th class	31	40
– qualification to enter a technical university	8	5
– qualification to enter a university	37	27
– no qualifications	0	1
Level of education (%):		
– in education, no school qualification or semiskilled worker	2	4
– skilled worker	31	37
– technical college leaving exam,	17	30
– technical university or university qualification	50	29
Physical stress at the workplace (%):		
– light	57	62
– moderate	31	34
– intense	12	4
Alcohol consumption (g/d)	17,0 (7.6–30.3)*2	5,0 (1.9–10.3)*2

*1 Means, standard deviations in brackets;
*2 Median (25th percentile to 75th percentile)

TABLE 3

Relative risks (and 95% confidence intervals) for type 2 diabetes depending on BMI and waist circumference in the EPIC Potsdam Study*1

		Relative risk (95% confidence interval)		
		BMI (per 1 kg/m^2)	Waist (per 1 cm)	Interaction term (per 1 cm kg/m^2)
Men	Model 1	1.21 (1.19–1.23)	–	–
	Model 2	–	1.08 (1.08–1.09)	–
	Model 3	1.02 (0.97–1.08)	1.07 (1.05–1.10)	–
	Model 4	1.43 (1.21–1.68)	1.17 (1.12–1.22)	0.997 (0.996–0.998)
Women	Model 1	1.15 (1.14–1.17)	–	–
	Model 2	–	1.08 (1.07–1.08)	–
	Model 3	0.95 (0.92–0.99)	1.10 (1.08–1.12)	–
	Model 4	1.32 (1.18–1.49)	1.20 (1.16–1.24)	0.997 (0.996–0.998)

*1 Relative risks calculated from Cox proportional hazard regression with age as time at risk, stratified by age and adjusted for height, smoking habits, alcohol consumption, physical activity, level of education, highest school-leaving exam and physical stress at the workplace, additionally in model 1, BMI; model 2, waist circumference; model 3, BMI and waist circumference; model 4, BMI, waist circumference and BMI×waist circumference

TABLE 4

Relative risks (and 95% confidence intervals) for type 2 diabetes in dependence on waist circumference, stratified by BMI*1

	Relative risk (95% confidence interval) per 1 cm higher waist circumference		
	BMI <25	BMI 25 – <30	BMI ≥30
Men	1.13 (1.06–1.20)	1.09 (1.07–1.14)	1.06 (1.04–1.08)
Women	1.11 (1.06–1.17)	1.11 (1.08–1.14)	1.05 (1.04–1.07)

*1 Relative risks calculated from Cox proportional hazard regression with age as time at risk, stratified by age and adjusted for height, smoking habits, alcohol consumption, physical activity, level of education, highest school-leaving exam and physical stress at the workplace

included in the regression model as continuous variables, either separately (models 1 and 2), or together (model 3), or with an additional interaction term (model 4). The relative risks were then calculated on the basis of the categories of BMI and waist circumference. The absolute risk of developing diabetes within five years was calculated from the multivariable adjusted survival time function of the Cox proportional hazard regression. The sex-specific arithmetic means for the cohort were taken for each covariable.

The statistical analyses were performed with SAS versions 9.1 and 9.2 (SAS Institute, Cary, NC). Two-tailed p values were taken.

Results

On recruitment, the mean age of the men was 52 years and of the women 49 years; the mean BMI of the men was 26.9 kg/m^2 and of the women 25.6 kg/m^2; the mean waist circumference of the men was 94.4 cm and of the women 80.2 cm *(Table 2)*. The men were on average better educated, performed more intense physical work, smoked more, and consumed more alcohol than women. Physical activity of the two sexes was about the same.

During the mean follow-up period of about 8 years, type 2 diabetes was diagnosed for the first time in 583 men and 425 women. There were statistically significant associations between both BMI and waist circumference ($p<0.0001$) and the risk of type 2 diabetes in separate models *(Table 3)*. A one unit (1 kg/m^2) higher BMI was associated with an increase in relative risk by 21% in men (1.21; 95% confidence interval [CI] 1.19–1.23) and by 15% in women (1.15; 95% CI 1.14–1.17) (model 1). A 1 cm higher waist circumference was associated with an increase in relative risk of type 2 diabetes of 8% in both men (1.08; 95% CI

TABLE 5

Relative and absolute risks for type 2 diabetes with waist circumference above or below the sex-specific median of the cohort in the three BMI categories (cross-classification)

		BMI <25	BMI 25 – <30	BMI ≥30
Men	Waist ≤ Median (≤ 94 cm)			
	Cases/Number of persons	37/2815	70/2257	1/11
	Relative risk (95%CI)	1.00 (reference)	2.26*[2] (1.5– 3.37)	6.62 (0.90–48.97)
	Absolute risk (5 years)*[1] (%)	0.79	1.80	5.29
	Waist > Median (> 94 cm)			
	Cases/Number of persons	8/150	211/2925	256/1595
	Relative risk (95%CI)	3.62*[2] (1.67–7.83)	4.98*[2] (3.50–7.09)	11.86*[2] (8.36–16.82)
	Absolute risk (5 years)*[1] (%)	2.95	3.92	9.00
Women	Waist ≤ Median (≤ 78.5 cm)			
	Cases/Number of persons	30/6905	7/997	0/7
	Relative risk (95%CI)	1.00 (reference)	1.40 (0.61–3.19)	0 (no cases)
	Absolute risk (5 years)*[1] (%)	0.28	0.39	0
	Waist > Median (> 78.5 cm)			
	Cases/Number of persons	18/1150	144/4010	226/2422
	Relative risk (95%CI)	2.74*[2] (1.52–4.94)	6.15*[2] (4.12–9.18)	15.80*[2] (10.69–23.35)
	Absolute risk (5 years)*[1] (%)	0.78	1.72	4.34

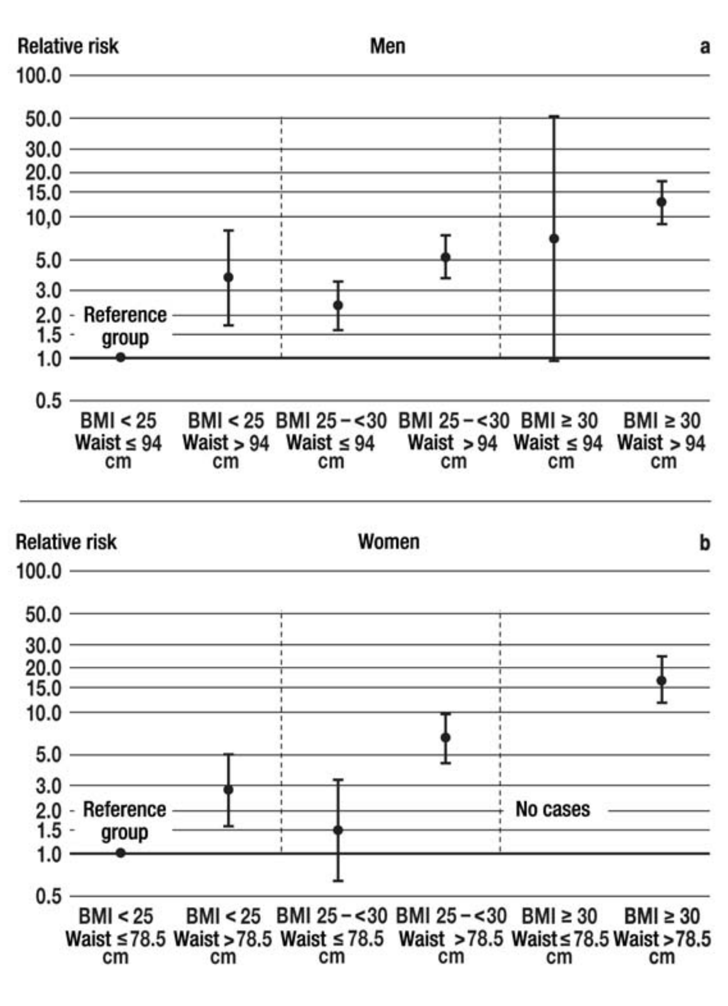
The reference category for the calculation of the relative risk was the sex-specific group with waist circumference under the median and BMI < 25, RR was stratified by age and adjusted for height, smoking habits, alcohol consumption, level of education, highest school-leaving exam and physical stress at the workplace.
*[1]Probability of diabetes in % within 5 years for category-specific mean properties. *[2] significant with p <0,05

1.08–1.09) and women (1.08; 95% CI 1.07–1.08) (model 2). An increase in BMI by the sex-specific standard deviation (3.5 kg/m^2 for men and 4.6 kg/m^2 for women) was associated with an increase in the risk of diabetes by 1.96-fold in men (95% CI 1.84–2.09) and 1.91-fold in women (95% CI 1.79–2.04). An increase in the waist circumference by the gender-specific standard deviation (9.9 cm for men and 11.2 for women) was associated with a 2.21-fold increase in risk of diabetes in men (95% CI 2.06–2.37) and a 2.31-fold risk increase in women (95% CI 2.15–2.48).

There was a close correlation between BMI and waist circumference (r = 0.82; p<0.0001). When these two parameters were considered together in the regression model, so that the influence of the other variable was removed from the calculation (mutual adjustment), waist circumference (p<0.0001), but not BMI (p=0.3802), was associated with the risk of diabetes in men (model 3). In the combined model with women, both BMI (p = 0.0066) and waist circumference (p<0.0001) were associated with the risk of diabetes, although there was an inverse relationship between BMI and diabetes risk. In other words, after removal of the effect of waist circumference, there was a negative relationship between BMI and diabetes risk. If an additional interaction term was included (model 4), this was found to be negative in both sexes, indicating a negative interaction between waist circumference and BMI (p<0.0001). This implies that the association between waist circumference and diabetes risk depends on the level of the BMI. In order to illustrate this interaction, BMI-stratified analyses were performed and the relationship between waist circumference and type 2 diabetes risk was examined for underweight or normal weight, pre-obese, and obese study participants *(Table 4)*. This confirmed that the strength of the association between waist circumference (in cm) and diabetes risk is smaller at greater values of BMI. Thus, for men with a BMI<25, the relative diabetes risk was increased by ca. 13% per cm waist circumference (p = 0.0002). However, for men with a BMI>30, the risk was only increased by ca. 6% (p<0.0001). For women with a BMI<25, the relative risk increase per cm was 11% (p<0.0001), but with a BMI>30, only ca. 5% (p<0.0001). To exclude the possibility that these observations are due to scaling phenomena, this calculation was also performed with percentage enlargements of the waist circumference. The increase in risk from waist circumference with increasing BMI was then less pronounced, although the difference was still statistically significant.

Finally, we cross-classified participants based on BMI and waist circumference and calculated the relative and absolute risk for small and large waist

FIGURE



Relative risk of type 2 diabetes in men and women in dependence on BMI and waist circumference. The reference group are persons of BMI<25 and waist circumference ≤ median. The sex-specific median was 94 cm for men and 78.5 cm for women. The squares and circles signify relative risks and the error bars signify 95% confidence intervals, calculated by Cox proportional hazard regression, with age as time at risk, stratified by age and adjusted for height, smoking habits, alcohol consumption, physical activity, level of education, highest school-leaving exam and physical stress at the workplace. The relative risks were plotted on a logarithmic scale (y-axis).

circumferences within the three BMI catagories, taking the sex specific median (men: 94 cm, women: 78.5 cm) as the cut off. Participants with a BMI<25 and small waist circumference were taken as reference group *(Table 5, Figure)*. The results of this analysis further illustrate how the risk of type 2 diabetes increases with both BMI and waist circumference. The relative risk for the group with the largest waist circumference and the highest BMI, in comparison to the reference group was 12-fold greater in men and 16-fold greater in women (p<0.0001).

It is striking that men (n = 150) or women (n = 1150) who were of low or normal weight, but had a large waist circumference, had a 3.62-fold (men, p = 0.0011) or 2.74-fold (women, p = 0.0008) greater risk than persons of low or normal weight (BMI<25) and small waist circumference. On the other hand, men or women with pre-obesity (BMI 25 to <30), but a small waist circumference, exhibited a 2.26-fold (men, p<0.0001) or 1.40-fold (women, p = 0.4276) increase in risk in comparison with persons of low or normal weight and small waist circumference. The absolute risk of developing type 2 diabetes within five years for men or women of low or normal weight with large waist circumference was 2.95% (men) or 0.78% (women). The corresponding figures for pre-adipose individuals with small waist circumference were 1.80% (men) and 0.39% (women). The risk group with low or normal weight and large waist circumference made up 1.4% (men) or 4.3% (women) of the new cases of diabetes within the overall population.

The authors also performed their analyses with the waist-to-hip ratio (WHR) and the waist-to-height ratio (WHtR), which gave similar overall results.

Discussion

The present results from the EPIC Potsdam study underline the importance of determining both BMI and waist circumference to estimate the risk of type 2 diabetes, particularly for individuals of low or normal weight. Both parameters influence the risk of diabetes. Using BMI or waist circumference alone would lead to inadequate risk assessment.

BMI and waist circumference serve as parameters to estimate general or abdominal fat masses, respectively. It is assumed that the abdominal fat mass is of particular importance in the development of not only type 2 diabetes, but also of other chronic diseases, including cardiovascular diseases and some forms of cancer (14, 15). Thus, several studies have found that the waist circumference is a strong predictor of diabetes (6, e1). Moreover, recent studies in Germany have found high prevalences for obesity (23.9%) and increased waist circumference (39.5%; men>102 cm, women >88 cm) (16). There is, however, a strong correlation between the two parameters and the terms "general" and "abdominal" obesity are not mutually exclusive, but designate overlapping fat compartments. It is clear from our studies that the strength of the association of waist circumference with the risk of type 2 diabetes depends on BMI. Thus the relationship between waist circumference and the risk of type 2 diabetes is more marked at low BMI than at higher BMI. In individuals with low BMI, waist circumference is a more exact measure of visceral fat, as these individuals mostly possess less subcutaneous fat that may affect waist circumference. However, it is visceral fat which on the other hand greatly increases the risk of diabetes (4, 5, 17, 18). On the other hand, the biochemistry of subcutaneous fat is different from visceral fat (e1–e10) and there is even evidence that subcutaneous fat produces substances which may have a favorable effect on glucose metabolism (19). It is therefore presumably the quantity of subcutaneous fat which causes the negative interaction between waist circumference and BMI with respect to diabetes risk, as observed in our study. In addition, the musculature is an essential determinant of insulin sensitivity (20), so that, at a given fat mass, individuals with low muscle mass may have a greater risk of diabetes than those with larger muscle mass.

Another important result of our study is that the risk of diabetes is at least as high for individuals of low or normal weight with an above average waist circumference (men: >94 cm; women: >78.5 cm) as for pre-adipose persons with a smaller waist circumference. This group at risk is currently not mentioned in the guidelines on diabetes prevention of the German Obesity Society, the World Health Organization, or the American Diabetes Association *(Table 1)* (3). According to these guidelines, the risk of diabetes for individuals starts to increase with overweight or pre-obesity and only then is an additional measurement of the waist circumference recommended. Our results indicate that individuals of low or normal weight, but with increased waist circumference, should be recognized as a risk group and should be included in the corresponding guidelines. Although this group and its contribution to new disease were relatively small in our study, the increased risk could make a major contribution to the diabetes incidence at the level of the population (16, 21). Interestingly, we have recently demonstrated that there is a similar interaction between general and abdominal obesity for the risk of mortality (22). In the EPIC study, individuals of normal weight with large waist circumference exhibited an increased mortality risk. Thus, the relative risk in the highest to the lowest quintile of waist circumference in individuals of normal weight was 2.06 for men (95% CI 1.32–3.20) and 1.79 for women (95% CI 1.39–2.31) ($p<0.001$) (22).

In the present study, the median was selected as the limit between small and large waist circumference. Even though this limit is less than conventional risk limits (men: 102 cm; women: 88 cm), we found a clear increase in diabetes risk for individuals with high waist circumference. This is in accordance with the results of other studies, which show that even waist circumferences below the current limits are associated with increased risk of diabetes (e1, 23). Some organizations have already reacted by reducing the circumference limits within their guidelines (2, 24), although many guidelines still contain these limits (3) and they are used in routine clinical work. It is also reasonable to ask whether fixed limits make any sense at all, as it was shown that the diabetes risk increases continuously with increasing waist circumference (e1, 23, 25). One limitation of our results was that we were not able to consider any influence of a hereditary disposition to diabetes. A second limitation was that we did not perform our own laboratory diagnoses for diabetes.

In summary, the analysis shows that exact estimation of the type 2 diabetes risk requires measurement of both the BMI and the waist circumference. We advocate the inclusion of a risk group with BMI<25 and large waist circumference in the corresponding guidelines on diabetes prevention and advise against general reliance on the conventional waist circumference limits (men: 102 cm; women, 88 cm).

Conflict of interest statement

The authors declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

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KEY MESSAGES

- The strength of the association between waist circumference and type 2 diabetes risk depends on body mass index (BMI). The association is particularly strong at low BMI.
- BMI and waist circumference must be measured for exact risk assessment. This is particularly important for persons of low or normal weight.
- Individuals of low or normal weight (BMI<25) with a large waist circumference (men: >94 cm; women: >78.5 cm) have at least the same risk of developing diabetes as pre-obese individuals (BMI: 25 to <30) with small waist circumference.
- Individuals with a BMI<25 and large waist circumference should be included as a risk group in the guidelines for diabetes prevention.
- It is clear that current limits for waist circumference (102 cm for men and 88 cm for women) need to be changed.

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